spotlights

Heat Flow Stop and Go

This is cool: Los Alamos scientists Markus Hehlen and Alex Mueller have devised a thin-film heat switch—a layer of material that can go from thermally insulating to thermally conducting with the flip of a switch. It takes advantage of fluid motion to achieve its dramatic change in thermal conductivity.

Before a pot of water on a lit stovetop comes to a boil, the upper surface of the water can remain much cooler than the water closer to the burner. But once the water starts boiling, the fluid motion quickly distributes the heat throughout the water. Hehlen and Mueller's heat switch relies on a similar effect, using electrohydrodynamic technology to generate motion in a dielectric fluid, thereby improving heat conduction. But unlike boiling water, the dielectric fluid can be set in a thin layer that doesn't feel wet any more than a liquid-crystal display (LCD) screen does.

To make the heat switch, a dielectric fluid is sandwiched between two electrode plates. When a voltage is applied across the plates, charged particles within the fluid move in response, effectively stirring the fluid. Because of this motion, heat is transported across the thin fluid layer from one electrode to the other. When the voltage is switched off again, the fluid stops moving and greatly inhibits the heat flow. So if a heat switch is inserted between a hot region and a cold one, it can be made to preserve that temperature difference or not, with easy on-off electronic control.

Hehlen and Mueller designed and constructed a specially patterned electrode to make the dielectric fluid circulate smoothly between the electrodes, carrying heat from one to the other with every revolution. They achieved a factor of greater than 50 in conductivity change, converting a fluid that's normally nonconductive, similar to fiberglass insulation or fleece, into one that approaches the thermal conductivity of a metal.

Initially, these heat-switch films could be used in specialty applications, such as temperature control for satellite electronics—which can face the Sun one minute and the extreme cold of empty space the next. Then they might prove useful in thermal management of computers, other electronics, or even buildings—replacing conventional insulation with something thinner and more adaptable. Hehlen and Mueller also believe they can make their thin-film heat switches flexible enough to be used in temperature-controlled clothing, effectively allowing the wearer to switch between a light cotton tee and a wool sweater without having to change clothes.

In fact, the heat switches may someday enable compact, thin-film refrigeration to compete with today's bulky and noisy vapor-compression-based refrigerators and air conditioners. The trick will be to intersperse suitable electrocaloric material layers—which can be heated and cooled by the application of an electric field—between heat switch layers. By opening and closing the switches in sequence while alternately raising and lowering electrocaloric-layer temperatures to draw heat in and then push it away, it is possible to send heat out of a cold region, against its natural flow direction—analogous to sending a ship through a series of locks, uphill and overland across the Panama Canal.

Hehlen and Mueller put their heat switches to the ultimate test with a rough, first-ever demonstration of thin-film refrigeration and were able to achieve—wait for it—cooling by 0.1°C. That may not sound earth-shattering, and it doesn't prove thin-film refrigeration will be commercially viable any time soon.

"It just proves it works," says Hehlen. "And it proves the versatility of the heat switches."

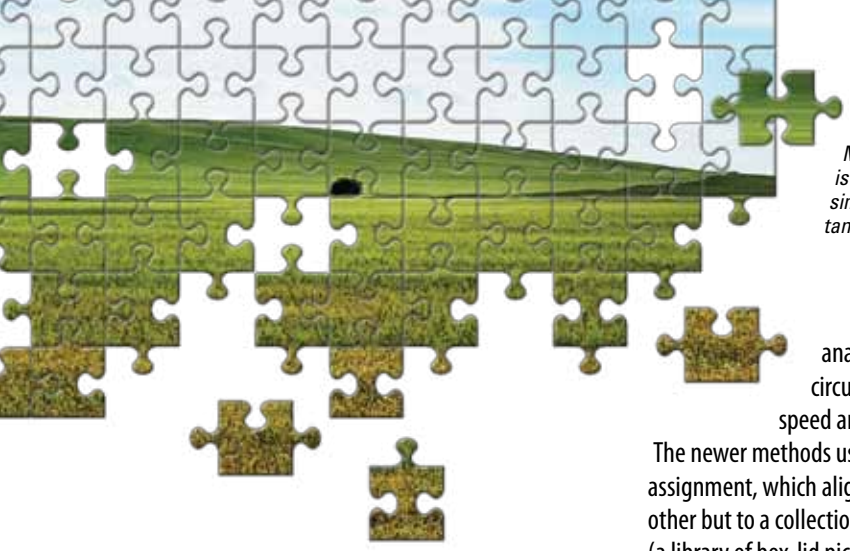
LDRD

—Craig Tyler

Microbiome References Required

Imagine a jigsaw puzzle with five billion pieces that shows a picture of a prairie. There are no buildings, no trees, and no people; there's just grassland and sky. Now imagine that you have a dozen such puzzles—one of a prairie in Kansas, another in Iowa, maybe a Canadian prairie for good measure—and all 60 billion puzzle pieces are together in one bag. Without the pictures from the box lids and without knowing how many puzzles there are, you must assemble them all correctly and simultaneously. How are you supposed to tell the difference between *this* piece showing blue sky and *that* piece showing blue sky? Or determine whether a particular patch of grass is from Kansas or Iowa? This, says Los Alamos bioinformatics expert Patrick Chain, is the challenge of metagenomics.

Metagenomics is the field of genetics concerned with the genomic sequencing of microbial communities, the members of which cannot be easily isolated from one another. For example, the human microbiome consists of the hodgepodge of microorganisms (mostly bacteria) that live on and within human bodies. Presently in vogue, this microbiome is increasingly being shown to influence our health,



Metagenome assembly is like building dozens of similar jigsaw puzzles simultaneously.

including development, hormonal regulation, and immune system training.

But the human microbiome is exceedingly complex. Our bodies contain roughly ten times more microbial cells than human cells, and we know hardly anything about them. Furthermore, no two sites on the body seem to have the same microbial mix; metagenomic samples from the throat are different than those from, say, the skin or gastrointestinal tract. To better understand what they all do and how they affect us, Chain and other members of the National Institutes of Health's Human Microbiome Project (HMP) are sequencing and studying their genomes.

Metagenomic analyses typically use either assembly-based or reference-based methods. In assembly-based analysis, as with solving a jigsaw puzzle, each 100-character-long snippet of a DNA sequence, called a "read" (puzzle piece), is compared to every other read (every other puzzle piece) to identify where its unique sequence connects to the sequence of an adjacent piece (the big picture). Reads are assembled together and further analyzed to reveal the species and genetic composition of the metagenomic sample. Because comparisons are conducted between every possible pair of reads, assembly-based methods have the benefit that they do not require a reference sequence (box-lid picture). The drawback, however, is a major cost to accuracy and speed—reads from two closely related species can be impossible to assign to one genome bin or the other, and the pairwise comparison of 60 billion reads is computationally intensive and limited by technology.

Chain is using new analysis methods that circumvent some of the speed and accuracy challenges. The newer methods use reference-based assignment, which aligns reads not to each other but to a collection of reference sequences (a library of box-lid pictures) to place them into the correct bin. Reference-based mapping is much faster and can be more accurate than assembly-based methods, but the hitch here is that it requires references. "If you want to use a reference-based approach, you've got to do your due diligence," he says. "You've got to generate reference sequences to optimize your data's utility."

But how many references are required? To answer that question Chain and his Los Alamos collaborator Gary Xie are characterizing the composition and fluctuation of the human microbiome. As it turns out, not only do microbiomes vary from person to person and site to site, but they are dynamic and can change from one sampling to the next. Using a library of 2780 reference genomes to analyze personal metagenomes (collective genomes of all microbial species in a single person's microbiome) from repeated sampling of multiple body sites of study volunteers, they found that, on average, only about 60 percent of the reads mapped to a reference sequence. That means the collection of available references is inadequate for identifying a large proportion of the bacteria living within us—40 percent of the data are orphaned. Further, it suggests scientists know far less than they thought they did, calling into question the general application of many contemporary studies, especially those that draw broad microbiome conclusions from a narrow sampling of subjects.

To increase the utility of microbiome data and the depth of our understanding of the human microbiome, Chain and Xie say more reference sequences are needed, and they ought to be organized by body site. A general estimate is that only about one percent of all bacterial species genomes are available as reference sequences. And while producing new references still relies on the cumbersome assembly-based methods, each newly generated sequence goes into a public database where anyone who cares to can access it. In this way, new microbiome data produce maximal bang for the researcher's buck. Generating hundreds of thousands of reference genomes is no small feat, but given the potential medical implications of the one percent we know about so far, it is undoubtedly worth it.

—Eleanor Hutterer

Sounds Like Better Weather

Like most people, Los Alamos geophysicist Stephen Arrowsmith enjoys listening to the sound of the ocean. The difference is, he does it from thousands of miles away and doesn't use his ears. Instead, he measures the infrasound (sound below the frequency threshold for human hearing) generated by distant, ever-present ocean waves. By comparing the arrival times of distinct wave sounds at different locations, and factoring in some computer modeling, he is able to infer information about the upper-atmospheric conditions through which the sound waves traveled—information that can be used to improve weather forecasts.

Weather models used in forecasting include high-altitude wind data obtained by one of two methods, and both have their problems. Snapshot-style monitoring, in which air conditions are sampled by instruments borne on high-altitude balloons or rockets, gathers information in particular locations at particular moments only. The alternative, continuous monitoring, requires a proliferation of expensive radar and lidar installations. (Lidar is radar with laser light instead of radio waves.) Arrowsmith's acoustic sensors are designed to hit the sweet spot in between: continuous atmospheric monitoring at low cost. And the price of hitting that sweet spot is the challenge of extracting information about atmospheric conditions from acoustical data.

In principle, the source of that data could be anything that generates infrasound; in fact, Arrowsmith and Los Alamos postdoctoral researcher Omar Marcillo were able to verify his system's performance using recorded infrasound from an unseen meteor event in 2010. But when there isn't a nice, sharp meteoric sound source, oceanic standing waves, which hum at a frequency about 100 times lower than the lowest bass note a human being could hear, provide a workable alternative because they are caused by storms and cyclones that are always present over some portion of the ocean. Yet the source of the sound isn't as important as the manner in which that sound is refracted through the atmosphere and down to his sensors on the ground by complex winds and temperature gradients. That's the weather data Arrowsmith wants.

Unfortunately, a variety of conditions could all lead to similar modulations of the sound. So Arrowsmith developed a computer system that works from an initial guess about atmospheric conditions and blends that with the infrasound time delays from a network of ground-based acoustic sensors to arrive at a most-likely estimate for the actual vertical profile of atmospheric conditions. Because upper-atmosphere winds and temperature gradients affect one another, the computer processing is iterative, repeatedly perturbing the presumed initial atmospheric profile and refining it until the system ultimately converges on an optimal solution. Under most test scenarios, the addition of the infrasound data and subsequent processing substantially improves the accuracy of atmospheric profile determinations and, importantly, does so without needing to know anything about the location or timing of the sound source.

So what part of the atmosphere should this new-and-improved method target for maximum forecasting utility? Currently, weather models are built with data from the troposphere, the lowest layer of the atmosphere, which ranges from sea level to over 10 kilometers in altitude. But Arrowsmith initially set his sights on the next, loftier target, the stratosphere—where the ozone layer absorbs solar ultraviolet light, causing temperatures to rise with altitude up to about 50 kilometers. He intended to improve upon weather models by better characterizing stratospheric airflows, which are known to affect the troposphere in a number of ways.

"We chose the stratosphere specifically because it's so complicated and difficult to sample by any other means," says Arrowsmith, "and because we know that mixing between the layers is important. But as I started talking with numerical weather prediction modelers, they told me that similar measurements in the troposphere may be just as useful, if not more useful, because they are currently limited by their periodic, snapshot radio measurements. So now we're looking at both layers."

How soon and how widely his new infrasound technique will be adopted to improve weather forecasts for everyone will depend on establishing a cost-benefit relationship to quantify how much better the forecasts will get with infrasound measurements figured in. It's what he and Marcillo are working on right now. LDRD

—*Craig Tyler*

Los Alamos infrasound sensors gather data on conditions in the stratosphere (and below) to improve weather prediction.

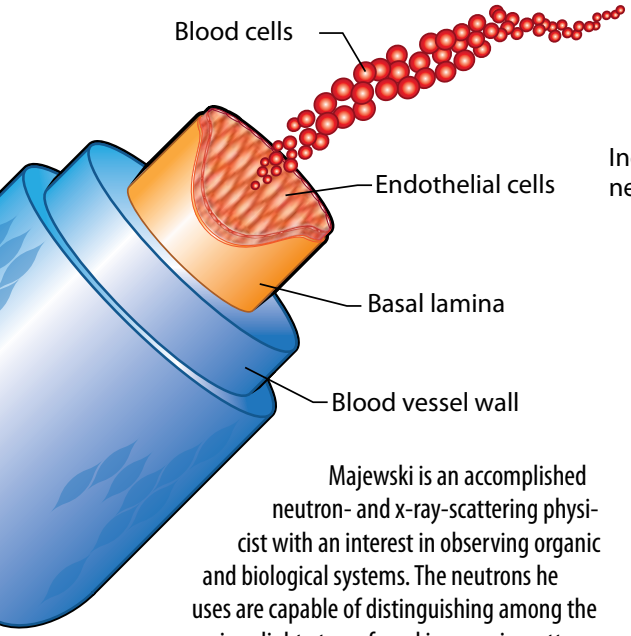
The New Vascular View

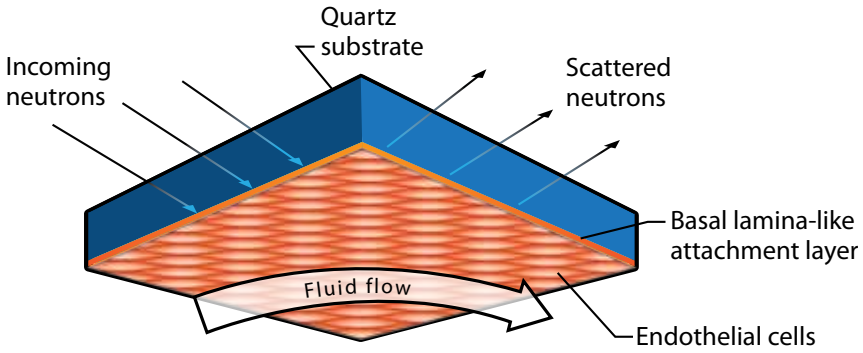
The cells in your body do not live in a Petri dish; they live amidst the frantic bustle of the body's interior. They are stretched and squeezed by nearby muscles, bounced about as you walk, and prodded by the coming and going of blood cells. As a result of all this jostling, most of them must work to stay anchored to the surrounding tissue with an ongoing series of adjustments, involving the secretion of adhesive collagen and other connective-tissue proteins, that goes largely unsung. And it goes largely unstudied, too, mainly because of how difficult it is to make the necessary measurements inside a dynamic, fluid-driven, and biochemically active system.

Recently, however, Jarek Majewski and Ann Junghans of the Los Alamos Neutron Science Center (LANSCE) took a remarkable first step to remedy that, characterizing key adhesive properties of cells and obtaining new insights into the workings of the human body in the process.

"We use a beam of neutrons to inspect living endothelial cells and their adhesive mechanism," explains Junghans. Endothelial cells line the interior of the entire vascular system—arteries, veins, capillaries, and the heart itself—in a layer that's always one cell thick. These endothelial-cell monolayers provide a smooth, low-friction surface to support the flow of blood while conducting blood-borne oxygen and nutrients out into surrounding tissues. They stand between rushing blood on one side and, on the other, a collagen-rich layer called the basal lamina, which affixes them to the blood vessel wall.

If endothelial cells become stressed or damaged, it's almost always life-threatening; a resultant atherosclerosis, for example, leads to blood clots that can cause heart attacks or strokes. Yet for these cells, mechanical drag from the flowing blood is a constant fact of life, making their ability to adhere to the vascular walls particularly important—and, as Junghans points out, making them particularly promising as a target for cell-adhesion research. Unfortunately, neither traditional x-ray imaging nor fluorescence microscopy provides much practical insight into their adhesive properties.





Endothelial cells line the inner walls of blood vessels, where they adhere tightly to resist the shear force from the flowing blood. New neutron-reflectometry research at Los Alamos reveals for the first time how they do it.

Majewski is an accomplished neutron- and x-ray-scattering physicist with an interest in observing organic and biological systems. The neutrons he uses are capable of distinguishing among the various light atoms found in organic matter without causing any damage to living cells—an improvement over x-rays on both counts. And their reflective properties make them ideal for probing the characteristics of thin-layer interfaces, such as the endothelial-cell monolayer and its basal lamina, at fine resolution. Majewski and Junghans grew the cell monolayer on a quartz substrate, where the cells began to attach themselves by secreting a complex blend of collagen and other proteins, thereby forming the basal lamina-like layer. They then installed a channel through which a bloodlike fluid would flow across the open side of the endothelial cells.

"We couldn't use real blood because we needed it to be heavy water-based—H_2O using a heavy isotope of hydrogen—for contrast, so the neutrons could distinguish the hydrogen in the cells from the hydrogen in the blood," Majewski notes. "So we created in heavy water a blend of salts, sugars, and other nutrients to nourish the cells while they are exposed to the neutron beam."

Once turned on, the neutron beam penetrates the quartz substrate and continues successively into the basal-lamina layer, the endothelial-cell layer, and the "blood." At each interface, some neutrons reflect toward the detector, which records their time of flight, while others penetrate deeper. A little mathematical manipulation then allows Junghans and Majewski to combine the detected neutrons' time of flight with the known neutron-reflecting properties of the atoms in each layer to determine the thickness of the basal lamina and how the endothelial cells respond to shear forces from the blood flow.

When the experiment is carried out at room temperature as a control—well below body temperature and too cold for most human cellular activity—turning on the blood flow induces a fluid-mechanical suction that tends to pull the endothelial cells away from the substrate and stretches the basal lamina layer. The amount of stretch is as expected, based on the elastic properties of collagen. So no surprises yet.

But when the experiment is performed at body temperature, the cells are fully active. Before the simulated blood flow is turned on, the basal lamina layer expands, as the endothelial cells secrete additional collagen and other proteins. (In the body, these cells are always producing such structural proteins to replace those that are naturally swept away as they weaken.) But over several hours of blood flow, the basal lamina contracts until it is 3–4 times thinner, tightening against the suction from the moving blood. At the same time, the endothelial-cell layer itself sharpens, developing flatter surfaces on both the basal-lamina and blood-flow sides. Evidently, endothelial cells are not just inanimate blood-vessel linings; rather, they respond to mechanical stress by adjusting their shape, alignment, and adhesive protein production for optimal vascular function. These responses had never before been directly observed at nanometer length scales and with such accuracy.

"These are exactly the kinds of results you want when you do an experiment no one has ever tried before," says Junghans. "They are both reassuring and suggestive—replicating expected elastic behaviors to prove we're on the right track and indicating new mechanisms that could eventually inspire new medical treatments." Indeed, this experiment reflects the beginning of a new knowledge base not only for treating known endothelial-cell maladies like atherosclerosis, but possibly for treating a broader range of illnesses based on every cell's structural and adhesive activity.

A significant case in point: At the suggestion of a colleague, Junghans and Majewski repeated the experiment with glioblastoma cells—highly malignant brain-tumor cells. Like endothelial cells, these brain cells secrete proteins to improve their structural adhesion. But the neutron experiment showed that the cancerous cells do so differently than healthy cells, with somewhat weaker and more compressible adhesion characteristics. A full understanding of this difference may take some time to work out, but one early implication is clear: Any difference between cancer cells and healthy ones offers the potential for a targeted treatment. If cancer cells adhere more weakly, then it may be possible to selectively dislodge them.

"That's why it's so great to be on the forefront like this," says Junghans. "You never know what practical knowledge and life-saving treatments might ultimately come from the things you find."

—*Craig Tyler*